ORIGINAL RESEARCH PAPER

Radiology

"A CROSS SECTIONAL STUDY ON THE DIAGNOSTIC VALUE OF DIFFUSION WEIGHTED MAGNETIC RESONANCE IMAGING IN DIFFERENTIATION OF BENIGN AND MALIGNANT FOCAL LIVER LESIONS."

KEY WORDS: MRI; focal; diffusion; benign; liver; hepatic; cyst.

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ABSTRACT

OBJECTIVES: Focal liver lesions (FLL) are a group of heterogeneous pathologies ranging from solitary benign lesions to multiple metastases. The MRI imaging modality is most accurate in characterizing these lesions; especially Diffusion weighted imaging (DWI) sequence. The purpose of this study is to evaluate the role of DWI/ADC in detecting focal liver lesions and its further characterization. Also providing a quantitative cut off range of ADC to differentiate benign from malignant lesions.

METHODS: Hospital based cross-sectional study was conducted from September 2019 to September 2020. 94 patients with focal liver lesions which were identified by using different modalities like USG/ CT/ MRI/ Histopathology. All the liver lesions were subjected to DWI MRI and ADC mapping was performed from the same.

RESULTS: A total of 94 patients having focal liver lesions were identified, ADC values were calculated for the focal liver lesions, mean ADC values were as follows, HCC: 0.984+/-0.16x10-3mm2 /sec, hemangioma:1.8428±0.31x10-3mm2 /sec, hepatic cyst: 2.953+/-0.42x10-3mm2 /sec, metastasis:1.0468+/-0.12x10-3mm2 /sec, liver abscess: 0.9294+/-0.05x10-3mm2 /sec and hydatid cyst:3.06+/-0.30x 10-3mm2 /sec.

CONCLUSION: In our study based on qualitative and quantitative assessment of focal liver lesions on DWI, characterization of liver lesions was done. Differentiation between malignant and benign lesions was done by using ADC values with cut of range of 1.5 to 3.5 x 10-3mm2 /sec and 0.8 to 1.36 x 10-3 mm2 /sec for benign(excluding abscess) and malignant FLL respectively.

As ADC values of some of the benign lesions (abscess) were seen to overlap with ADC values of malignant lesions, hence in such cases clinical, classical imaging features of MRI and CT helps us to differentiate abscess from malignant FLL.

INTRODUCTION:

The liver is an organ in which various benign or malignant, primary or secondary focal liver lesions (FLL) can occur. FLLs are solid or cystic masses or areas of tissue that are identified as an abnormal part of the liver. The term "lesion" rather than "mass" was chosen because "lesion" is a term that has a wider application, including solid and cystic masses [1] . Focal liver lesions are group of heterogeneous pathologies ranging from solitary benign lesions to multiple metastases from a variety of primary tumors. With the advent of imaging modalities like USG, triple Phase CT-scan and MRI, the rate of detecting focal liver lesions has increased [2] . MR imaging has emerged as an important imaging modality for assessing and characterizing focal hepatic lesions. The introduction of faster sequences has allowed high quality imaging of the entire liver with high intrinsic soft tissue contrast. Because of lack of ionizing radiation, routine and gadolinium enhanced multiphasic imaging with high temporal and spatial resolution and fat suppression can be performed. The MRI imaging modality is most accurate in characterizing these lesions, especially DWI sequence. Molecular level of information of tissues which gives structural and functional information is obtained by DWI and also it helps in assessing the treatment response in tumor cells. DW MR imaging is an MR imaging technique that derives its image contrast on the basis of differences in the mobility of protons (primarily associated with water) between tissues. In tissues that are highly cellular (eg, tumor tissues), the tortuosity of the extracellular space and the higher density of hydrophobic cellular membranes restrict the apparent diffusion of water protons3-5 . DWI was primarily used in neuroimaging, to detect acute cerebral stroke 6 , demyelinating disease and intracranial tumors 7-10 . DWI measurements are less time taking (typically 1–5minutes) and do not require the administration of exogenous Introduction of contrast medium. Thus, DWI imaging sequence can be applied to the existing imaging protocols without a significant increase in the examination time. Furthermore, DWI yields both qualitative and quantitative information that can be helpful for tumor assessment.

With advances in imaging technique, diffusion-weighted (DW) MR imaging can now be applied to liver imaging with improved imaging quality12 . Tumour cellularity and the integrity of the cellular membrane can be assessed by the DWI. The technique can be applied widely for tumour detection and tumour characterization and for the monitoring of response to treatment. Quantitative reflection of diffusion is termed as diffusion coefficient. The molecular mobility of water molecules which intern depends on extracellular space, viscosity and cellularity is depicted in quantitative form as apparent diffusion coefficient (ADC)2 . Several studies have reported that the ADC, calculated parameter of DWI, is useful for differential diagnosis of the benign and malignant hepatic lesions. Diffusion weighted (DWI) MR imaging, combined with apparent diffusion coefficient (ADC) measurement is an important method for in-vivo quantification of the combined effects of capillary perfusion and diffusion13-15 . Reduction in mean ADC (low signal intensity on an ADC map) of malignant lesions is indicator of malignancy in focal liver lesions16 . However, ADC values often vary from one study to another partially related to different equipment and different bvalues16 . Thus MR imaging modality can be used to asses of FLL, in which DWI helps to differentiate benign and malignant FLL.

AIMS & OBJECTIVES:

1. To determine the role of diffusion weighted MR imaging in differentiating between benign and malignant hepatic lesions by calculating apparent diffusion coefficient (ADC) values. 2. Providing a quantitative cut off range of ADC value to differentiate benign from malignant lesions.

MATERIALS AND METHODS

The study was conducted in the department of Radio-diagnosis, S.P Medical College, Bikaner over a period of two years from September 2019 to September 2020. Study Design: The study design was a one year cross-sectional analytical study.

Study Period and duration: The study is being conducted over

period of two years from September 2019 to September 2020. Place: The present study was performed at department of Radio-diagnosis, S.P. Medical College, Bikaner. Source of data: Patients diagnosed with focal liver lesions by USG, MDCT and MRI abdomen and pelvis at P.B.M, Hospital, Bikaner.

Sample size: A total of 94 patients fulfilling the selection criteria were studied. Sample size: Is calculated by Buderer's formula: n=Z2 1-a/2 x SN x (100-SN) / L2 x Prevalence where n = required sample size, SN = anticipated sensitivity, SP = anticipated specificity, α = size of the critical region (1 − α is the confidence level), z1−α/2 = standard normal deviate corresponding to the specified size of the critical region (α), and L = Relative precision. Z 2 1-a/2 =1.96 (95% confidence) Sensitivity of the test = 91%[6] Prevalence = 5.8%[12] 1-SN = 1- 0.91 L (Relative precision) = 4% Then n is equal to ~ 30. 30 cases were given as sample size. In this two year study total 94 cases were studied as number of cases we got were more.

Selection criteria: Inclusion Criteria:- • Patients undergoing multimodality evaluation in our department found to have focal liver lesion. • Patients with diagnosed focal liver lesion through various methods (histopathology / LIRADS / Biochemical). • Patients of all age groups will be included in the study. Exclusion Criteria:- • Patients with metallic implants, cardiac pacemakers, cochlear implants. • Patients who are claustrophobic. Patients who are unwilling for imaging. • Patients with hepatic neoplasm's who have undergone chemotherapy or radiation therapy.

Methods:
Data collection: Once a patient fulfilled the inclusion criteria for this study he / she was administered the predesigned / pretested proforma (Annexure-II). Demographic characteristics of the study population such as age, sex were obtained through an interview. The patients were then briefed about the procedure i.e. about the noise of the gradient coils and need to control the body movements for successful image acquisition. Imaging: • Patients diagnosed with liver lesions underwent Diffusion weighted MR imaging using 3 T MRI at P.B.M Hospital, Bikaner.

Scan protocol:
The tests were performed using following parameters. • FOV – 350 to 400 (in adult) and 180 to 200 (in pediatrics) • Slice thickness – 4 to 5 mm • Matrix size – 512 x 512 • The following sequences were obtained: Spin-echo T1 weighted (Axial/Coronal), Spin-echo T2 weighted (Axial/Coronal), axial, coronal FIESTA and Single shot echo-planar imaging (axial) [DWI]. • Diffusion MR imaging will be done using single shot Echo Planar imaging (EPI) with b-value of 50, 500 & 1000 sec/mm2 . • The Apparent Diffusion Coefficient (ADC) values will be calculated by marking three regions of interest (ROI). • The mean ADC values will be calculated and correlated with results obtained on USG, contrast enhanced CT scan and Histopathology or other laboratory investigations which ever available.

***Statistical Analysis*:** The data obtained was coded and entered into Microsoft Excel Worksheet. The categorical data was expressed as rates, ratios, proportions and percentages. The continuous data was expressed as mean ±standard deviation. All tests will be considered significant if p value equals or less than 0.05.

RESULTS:
The data obtained was coded and entered into Microsoft Excel Worksheet. The categorical data was expressed as rates, ratios, proportions and percentages. The continuous data was expressed as mean ± standard deviation. ANOVA test and unpaired t test is used. The p-value of 0.05 or less is considered statistically significant. In the present prospective study 94 patients with focal liver lesions were included among them 68.1% (64 patients) were males and 31.9% (30 patients) were females.

This study includes patients from 21 to 80 years. Majority of the patients were in the age group of 51-60 years i. e 29 patients, with mean age of 53 years. The focal liver lesions included in the study are hemangioma, abscess, hepatic cysts, hydatid cysts, hepatocellular carcinoma and metastasis. Out of which most common focal liver lesion was hepatocellular carcinoma (26 cases), followed by hemangioma (21 cases), followed by hepatic cysts (15 cases) and others include metastasis (13 cases), abscess (10 cases) and hydatid cyst (9 cases).

In our study hemangioma are more commonly seen in age group of 41 – 50 years, hepatic cysts in 51- 60 years, abscess in 31-40 years, hydatid cyst in 51-60 years, metastases in 31-40 years and HCC in 51- 60years. In our study, out of 94 patients 55 patients were having benign lesions and 39 patients were having malignant lesions. Among the studied FLLs, all malignant lesions like HCCs and metastasis showed diffusion restriction. All benign lesions like hepatic cysts, hydatid cysts and hemangioma showed high signal intensity on both DWI and ADC, exception being hepatic abscess which showed diffusion restriction.

ADC values were calculated for all FLLs. The malignant lesions which showed diffusion restriction were HCC and metastasis with mean ADC value of 0.98 +/- 0.16 x 10-3 mm2 / sec and 1.04 +/-0.12 x 10-3 mm2 / sec. The ADC values ranged from 0.8-1.2 x 10-3 mm2 / sec and 0.8-1.3 x 10-3 mm2 / sec for HCC and metastasis respectively. All the lesions which showed diffusion restriction were malignant exception being abscess which showed mean ADC values of 0.92 +/- 0.05 x 10-3 mm2 / sec with range of 0.6 to 1.1 x 10-3 mm2 / sec. Benign lesion like hepatic cysts, hydatid cysts and hemangioma showed high signal intensity on both DWI and ADC with mean ADC values of 2.95 +/- 0.42 x 10-3 mm 2 / sec, 3.05 +/-0.30 x 10-3 mm 2 / sec and 1.84+/-0.31 x 10-3 mm 2 / sec respectively.

Mean ADC values of benign and malignant FLLs were calculated and were as follows, 2.1952 +/- 0.30 x 10-3mm2 /sec for benign and 1.015+/-0.14 x 10-3mm2 /sec for malignant FLLs.

The ADC values of benign focal liver lesions (excluding abscesses) ranged from 1.5 to 3.5 x10-3 mm2 /sec and malignant lesions ranged from 0.8 to 1.3 x10-3 mm2 /sec.

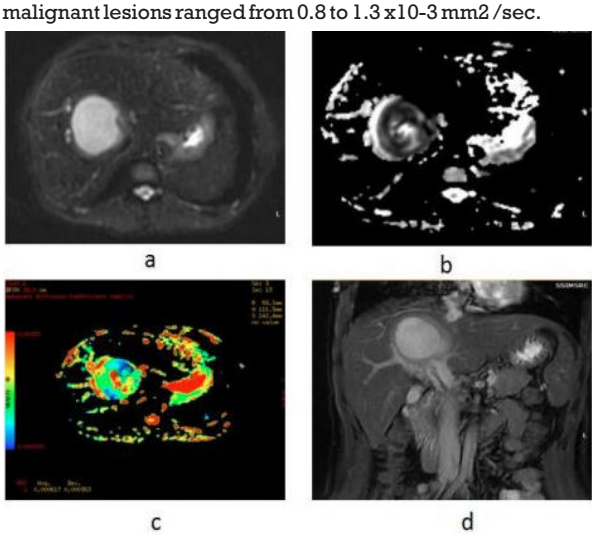

Figure 1: a) and b) DWI image showing well defined lesion which is showing diffusion restriction with ADC values of 0.61 x 10-3mm2 / sec. d) the lesion shows high signal intensity in T2WI. Case of hepatic abscess.

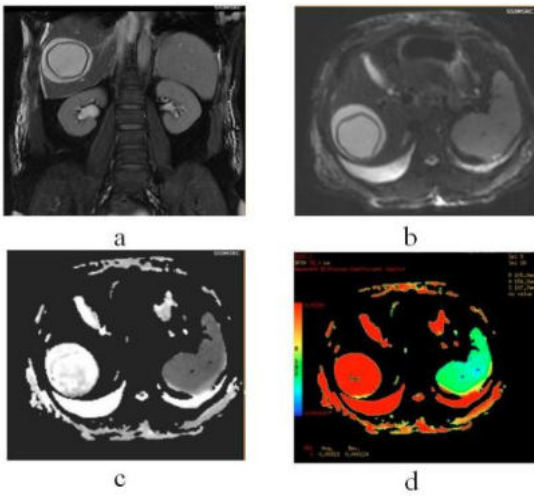

Figure 2: a) T2 WI shows well defined hyperintense lesion with hypointense ring shaped structure within it. b), c) and d) DWI image with ADC shows no restriction of lesion with ADC values of 3.1 x 10-3mm2 / sec. Case of hydatid cyst.

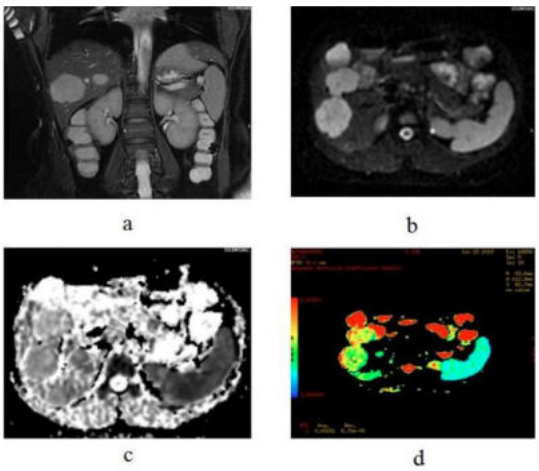

Figure 3: a) T2 WI showing well defined hyperintense lesion. b), c) and d) DWI image showing no diffusion restriction with ADC value of 1.5 x 10-3mm2 / sec. Case of hepatic hemangioma.

SUMMARY AND CONCLUSION:

Based upon these outcomes following conclusion could be reached: a. Based on qualitative and quantitative assessment of liver lesions on DWI and ADC map, we could characterize different liver lesions. In same way differentiation between malignant & benign lesions was done. DWI is a useful diagnostic tool in patients where contrast is contraindicated like in patients with renal impairment. Need of FNAC / biopsy for differentiating between benign and malignant lesion can be mitigated using DWI. DWI technique acts as powerful diagnostic tool. However DWI should always be interpreted with conventional MRI sequences due to overlap between ADC values of different liver lesions. b. This study recommends using ADC value range of benign (excluding abscess) and malignant lesions i. e 1.5 to 3.5 x10-3 mm2 /s and 0.8 to 1.3 x10-3 mm2 /sec respectively, by which we can differentiate benign from malignant focal liver lesions. c. Exception being hepatic abscesses, which revealed lower ADC values with mean of 0.9 x 10-3 mm2 /sec, which is overlapping with ADC values of malignant FLL. In such scenarios, clinical and classical imaging features of MRI and CT helps us to differentiate the abscesses from malignant FLL. d. Hence, DWI combined with ADC can be used as screening tool for detecting FLLs and as diagnostic tool for characterizing them as benign or malignant. e. DWI must be done both at low and high b values (0, 500 and 1000) for high sensitivity in detection of FHLs.

To summarize, in our set of 94 patients with focal hepatic lesions that we screened using DWI, we got following outcomes:

1) All malignant FLLs (n= 39) showed true restriction of diffusion on DWI and ADC map.
2) Out of 55 benign FLLs, 45 FLLs showed high signal intensity on both DWI and ADC map, while 10 FLLs showed areas of restricted diffusion on DWI and ADC map which were abscesses.
3) 26 out of the 39 lesions which were labelled as malignant based on imaging findings using MDCT and USG, underwent biopsy, all of which came out to be positive for malignancy.
4) The malignant FLLs showed low ADC values than that of benign FLLs.
5) The mean ADC value of benign and malignant lesions were 2.1952 ± 0.308 × 10-3 mm2 /s and 1.0155 ± 0.147 × 10-3 mm2 /s respectively.
6) The range of ADC values for malignant FLL were 0.8 × 10-3 mm2 /s to 1.3×10- 3 mm2 /s.
7) The range of ADC value of benign FLL's excluding abscess were 1.5 x10-3 to 3.5 x10-3 mm2 /s.
8) Using the range of ADC values of benign (except abscess) and malignant FLL's, i. e 1.5 x10-3 to 3.5 x10-3 mm2 /sec and 0.8 to 1.3 x10-3 mm2 /s respectively, we were able to differentiate benign from malignant lesions.
9) The 10 benign cases which showed restricted diffusion were abscesses. They revealed lower ADC values with mean of 0.9 x 10-3 mm2 /s, which is overlapping with ADC values of malignant FLL.

In such scenarios, clinical and classical imaging features of MRI and CT helps us to differentiate the abscesses from malignant FLL.

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